中文題目：Statin 類藥物治療對糖尿病前期患者的血糖生化指標之影響

英文題目：The effect of statin treatment on glucose homeostasis in subjects with impaired fasting glucose

作　　者：鄭菀韻[1]，陳涵栩[1,2]

服務單位：[1]臺北榮民總醫院內科部，[2]國立陽明交通大學醫學系

Background: Statin therapy effectively reduces cardiovascular events. However, meta-analyses suggested that statins also conferred an increased risk of development of diabetes. In order to elucidate whether statins increase risk of diabetes, we conducted this study to evaluate the effects of rosuvastatin (highest diabetogenic) and pravastatin (diabetic protective) on glucose homeostasis and other biomarkers in subjects with impaired fasting glucose.

Method: This is a prospective, randomized, open-labeled, controlled trial to assess the effects of statin on glucose homeostasis in pre-diabetic subjects. We assigned 41 subjects with impaired fasting glucose (IFG) with fasting blood glucose of 100-125 mg/dL, and excluded A1C ≥7.0%, 2hr blood glucose ≥200 mg/dL. Subjects with total cholesterol between 200-280 mg/dL were randomized to receive rosuvastatin 10 mg or pravastatin 40 mg. Subjects with total cholesterol less than 200 mg/dL were assigned to the control group. The primary endpoints were glucose level, insulin sensitivity, insulin resistance, and insulin secretion evaluated on oral glucose tolerance test (OGTT) at baseline and 6th month, with a target of total cholesterol to 160-180 mg/dL. Glucose homeostasis was evaluated with HbA1C, HOMA-IR, HOMA-beta, and OGTT-derived indices including early-phase insulin secretion, area under curve (AUC) for glucose and insulin, Matsuda index, and total insulin secretion. The aim of this study is to evaluate the effect of statin treatment on glucose homeostasis in subjects with impaired fasting glucose.

Results: This study screened 141 subjects with impaired fasting glucose from January 2011 to May 2022 and 41 patients were recruited. Twenty-two subjects with total cholesterol between 200 and 280 mg/dL were randomized to either rosuvastatin group (N=11) or pravastatin group (N=11). There were 19 subjects with total cholesterol levels less than 200 mg/dL were served as control group.

Demographics and baseline characteristics except for total cholesterol and triglyceride were similar among the three groups. The control group had lower total cholesterol (171.6±15.0 mg/dL) and triglyceride (87.0 mg/dL, IQR [69.5, 106.8]) than the two intervention groups, but there were no significance differences between the rosuvastatin and pravastatin group (total cholesterol 246.5±21.8 mg/dL vs. 232.6±14.2 mg/dL); triglyceride (181.6 mg/dL [98.0, 291.5] vs. 131.2 mg/dL [89.0, 155.0]).

After 6 months of statin treatment, the metabolic characteristics had no significant difference among the three groups, including total cholesterol and triglyceride. The two intervention groups had a significant decreased of total cholesterol from 246.5±21.8 mg/dL to 175.4±32.3 mg/dL in the rosuvastatin group ($p<0.001$) and from 232.6±14.2 mg/dL to 189.6±18.3 mg dL in the pravastatin group ($p<0.001$). In the intervention groups, the median triglyceride level non-significantly decreased from 181.6 mg/dl [98.0, 291.5] to 94.0 mg/dl [83.3, 118.3] in the rosuvastatin group ($p=0.091$), increased from 131.2 mg/dl [89.0, 155.0] to 143.5 mg/dl [80.0, 212.0] in the pravastatin group ($p=0.686$), and increased from 87.0 mg/dl [69.5, 106.8] to 121.0 mg/dl [92.0, 181.0] in the control group.

After sixth months of statin treatment, the mean HbA1C in the placebo, rosuvastatin and pravastatin group were 5.98±0.46%, 5.87±0.33%, 5.86±0.25% respectively

(p=0.628). HOMA-IR were 2.37±1.14 in the control group, 3.40±0.97 in the rosuvastatin group and 2.07±0.71 in the pravastatin group. Treatment with rosuvastatin had a significantly higher (p=0.008) HOMA-IR than the control group. The Matsuda index were 3.93±1.82, 2.55±1.16, 4.11±2.19 in the control, rosuvastatin and pravastatin group respectively, with a significantly lower index level in the rosuvastatin group compared with control group (p=0.032) and pravastatin group (p=0.049). There were no significant differences in other glucose homeostasis indices over HbA1C, HOMA-beta, early-phase insulin secretion, insulin AUC, glucose AUC, and total insulin secretion at post-treatment.

Conclusion: In our study, after 6 months of statin treatment the total cholesterol levels were nearly the same among the three groups. Rosuvastatin treatment may be associated with an increase in insulin resistance with compensation of increase insulin secretion, which resulted in no significant changes in HbA1C at short-term use of statin therapy.